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Evaluation of D-dimer and fibrinogen levels in COVID-19 patients

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Abstract

Aim: The aim of this study is to determine D-dimer and fibrinogen levels in COVID-19 patients and to evaluate their correlation with in-hospital mortality.

Material and Methods: Patients aged 18 years and older who applied to the emergency and/or pandemic outpatient clinic of our hospital and were hospitalized and whose COVID-19 PCR test was positive were included. Demographic data, vital and physical examination findings, laboratory values including D-dimer and fibrinogen levels were recorded. P <0.05 was considered statistically significant.

Results: Patients with increased D-dimer value were found to have higher age, higher rate of chronic kidney disease, higher fever and pulse values, lower saturation measurements, longer duration of the complaint, more severe pneumonia, longer hospital stay, greater requirement for mechanical ventilation and intensive care ($p<0.05$ for all values).

It was observed that the patients with increased fibrinogen were older and the duration of complaints was longer. When the laboratory values of the patients with and without fibrinogen increase were compared, it was determined that neutrophil, CRP and sedimentation values of the patients with increased fibrinogen were lower ($p<0.05$ for all values).

Discussion: In our study, we demonstrated that D-dimer levels measured at admission and during follow-up were higher in the deceased patients than in the surviving ones. We did not detect any clinical association between admission and follow-up fibrinogen levels and mortality in the deceased patients as compared with the surviving ones.

Keywords
COVID-19, D-dimer, Fibrinogen

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Introduction

COVID-19 is a global pandemic caused by SARS-CoV-2 infection [1, 2]. The number of people infected by SARS-CoV-2 continues to rise on a global scale. Developing novel laboratory tests that would aid the diagnostic and follow-up processes in COVID-19 patients is very important not only for making the diagnosis, but also for distinguishing between severe and non-severe cases, and patients at low and high mortality risk. Mortality and morbidity of the COVID-19 infection have been rising.

Varying degrees of respiratory failure, cardiovascular complications, secondary infections, thromboembolic events, and inflammatory complications may develop in affected patients [3]. The risk of thrombosis increases in the course of COVID-19 [4, 25]. Although the cause of hypercoagulopathy in COVID-19 patients has yet to be fully elucidated, the basic mechanisms first defined by Virchow are considered to be operational [6]. Direct invasion of endothelial cells by the virus, cytokines, mainly Il-6, triggering a systemic inflammatory response, and intravascular catheters widely used for patient follow-up are the main causes of endothelial injury [6]. Elevated factor VIII and fibrinogen levels, prothrombotic microparticles, neutrophil extracellular traps, and hyperviscosity cause hypercoagulopathy. In addition, immobilization during intensive care also increases vascular stasis, independently of the COVID-19 disease [6-8]. A hypercoagulable state, which increases the risk of venous and arterial thromboembolism due to the above-mentioned factors, is termed COVID-19-associated coagulopathy. Despite marked increases in fibrinogen and D-dimer levels, PT (prothrombin time) and aPTT (activated partial thromboplastin time) are normal or slightly prolonged. Platelet count is variable [3]. Excessively elevated D-dimer level is remarkable and associated with poor prognosis. It has been observed that D-dimer levels were significantly higher in patients treated in the intensive care unit than other patients [9]. It was shown that D-dimer could be an early and useful marker that would improve the management of COVID-19 patients [10]. Indication algorithms for the administration of anticoagulant agents in COVID-19 patients are not clear. This situation may cause difficulties in the implementation of the diagnosis, follow-up and treatment procedures of COVID patients. Herein, we aimed to investigate admission and follow-up D-dimer and fibrinogen levels of COVID-19 patients, factors associated with their elevated levels, and their relationship with in-hospital mortality.

Material and Methods

The present study is a retrospective, observational study. It was approved by the local ethics committee (23.02.202, 2012-KAEK-15/2229). Patients aged 18 years or older with a positive COVID-19 PCR test who were hospitalized in Keçiören Training and Research Hospital between 01.08.2020 and 30.11.2020 were enrolled in the study. The demographic data, admission complaints, comorbidities, time of admission, vital and physical examination findings, laboratory studies including D-dimer and fibrinogen levels measured at admission and during follow-up, chest X-Ray/tomographic imaging findings, disease-related thromboembolic (deep vein thrombosis (DVT) and pulmonary embolism) events, if any, and length of hospital stay were recorded for all patients. The patients were grouped as the deceased and surviving patient groups based on their in-hospital mortality status. The patients were additionally grouped by their D-dimer and fibrinogen levels. They were further divided into two groups based on the difference between the admission D-dimer, fibrinogen levels and 5th day D-dimer and fibrinogen levels, as those with elevated levels of the said parameters and those without. Patients with missing data and a negative PCR test were excluded from the study.

Statistical Analysis

Data obtained during the study period and recorded on study forms were analyzed with IBM SPSS 20.0 (Chicago, IL, USA) statistical software package. The Kolmogorov-Smirnov test was used to check if discrete and continuous variables were normally distributed. Descriptive statistics included the median (interquartile range 25-75) for discrete and continuous numerical variables, and number of cases and percentage (%) for categoric variables. Categoric variables were analyzed using the Chi-square test, and continuous variables using the Mann-Whitney U test. Receiver operating characteristic (ROC) analysis was performed for fibrinogen and D-dimer levels, in which the curves' area under the curve (AUC) values were calculated to distinguish between deceased and surviving patients.

A p-value of less than 0.05 was considered statistically significant for all statistical analyses.

Results

The data of 1997 patients who were enrolled during the study period were analyzed. Five hundred and eighty-six patients were excluded due to a negative PCR test plus 40 patients due to missing data. A total of 1371 patients were enrolled in the study. Of the patients who were enrolled, 53.7% were male (N=736); the median age of the study population was 63 (IQR 52-72) years. The most common comorbidity was hypertension (54.9%). The median length of hospital stay was 7 days (IQR 5-11 days). The in-hospital mortality rate was 10.3% (141). Table 1 shows the demographic data of the study population.

The ROC analysis that was performed to determine a cut-off value for D-dimer level for distinguishing between deceased and surviving patients had an AUC value of 0.695 (95% CI 0.649-0.741; p<0.001) (Figure 1). A D-dimer level of 1475 that was accepted as the best cut-off value to discriminate between deceased and surviving patients had a sensitivity of 42% and a specificity of 89%. There were 1072 patients whose D-dimer level was measured at admission and five days later. The fifth day D-dimer level was higher than the admission D-dimer level in 7.9% of the patients. A comparison of the patients with and without D-dimer elevation indicated that the patients with elevated D-dimer levels had higher median age, higher rate of chronic kidney disease, higher body temperature and pulse rate, lower oxygen saturation, longer duration of symptoms, more severe pneumonia, longer hospital stay, and greater requirement for ventilation and intensive care (p<0.05 for all comparisons) (Table 2).

In 438 patients, fibrinogen levels were measured at admission and five days later. The fifth day fibrinogen level was higher than the admission D-dimer level in 50.5% of the patients. The ROC analysis to determine a cut-off level for fibrinogen to distinguish between deceased and surviving patients had an

Table 1. Demographic data of the study population (n=1371)

Age, median (IQR 25 -75)	63 (52-72)
Gender, n (%)	
Female	635 (46.3%)
Comorbidity, n (%)	
Hypertension	619 (54.9%)
Diabetes	426 (31.1%)
Coronary Heart Disease/CHF	281 (20.5%)
Chronic Obstructive Pulmonary Disease	163 (11.9%)
Chronic Kidney Disease	62 (4.5%)
Other	113 (8.2%)
Symptom duration, Median (IQR 25-75)	4 (3-6)
Vital Signs, median (IQR 25 -75)	
Fever	37.1 (36.3-38.0)
Pulse rate	79 (71-88)
Saturation	90 (88-93)
Pneumonia status, n (%)	1273 (92.9%)
Pneumonia severity, n (%)	
Pneumonic involvement more than 50%	375 (27.4%)
Pneumonic involvement less than 50%	898 (65.5%)
Requirement of mechanical ventilation, n (%)	132 (9.6%)
Length of hospital stay, Median (IQR 25-75)	7 (5-11)
ICU requirement, n (%)	151 (11%)
Mortality, n (%)	141 (10.3%)
Laboratory Median (IQR 25-75)	
D-dimer, ng/ml	650 (390-1230)
D-dimer 5. Day, ng/mL	570 (340-1110)
Fibrinogen, mg/dl	497 (400-621)
Fibrinogen 5. Day, mg/dl	451 (358-578)

CHF: Congestive heart failure, CT: Computerized tomography ICU: Intensive care unit

Table 2. Comparison of the data of COVID-19 patients with and without D-dimer elevation (n=1072)

	Absence of D-dimer elevation (n:993)	Presence of D-dimer elevation (n:79)	P-value
Age, median (IQR 25-75)	64 (51.5-72)	66 (57-75)	0.40
Gender, n (%)			
Female	466 (46.9%)	31 (39.2%)	0.187
Comorbidity, n (%)			
Hypertension	437 (44%)	43 (54.4%)	0.073
Diabetes	311 (31.3%)	25 (31.6%)	0.952
Coronary heart disease	211 (21.2%)	21 (26.6%)	0.268
Chronic obstructive pulmonary disease	117 (88.2%)	10 (12.7%)	0.817
Chronic kidney disease	40 (4%)	9 (11.4%)	0.007
Vital signs, median (IQR 25-75)			
Fever	37 (36.2-38)	37.3 (36.5-38)	0.016
Pulse rate	78 (71-88)	86 (73-100)	<0.001
Saturation	91 (89-93)	90 (81-92)	<0.001
Symptom duration median (IQR 25-75)	4 (3-6)	5 (3-7)	0.40
Pneumonic involvement more than 50%, (%)	258 (26%)	35 (44.3%)	<0.001
Length of hospital stay median (IQR 25-75)	7 (5-10)	11 (7-17)	<0.001
Requirement of mechanical ventilation, n (%)	69 (6.9%)	29 (36.7%)	<0.001
Requirement of ICU care, n (%)	87 (8.8%)	28 (35.4%)	<0.001
Length of stay in ICU median (IQR 25-75)	12 (4-20)	11 (6-21)	0.674
In-hospital mortality n (%)	68 (6.8%)	31 (39.2%)	<0.001

ICU: Intensive care unit

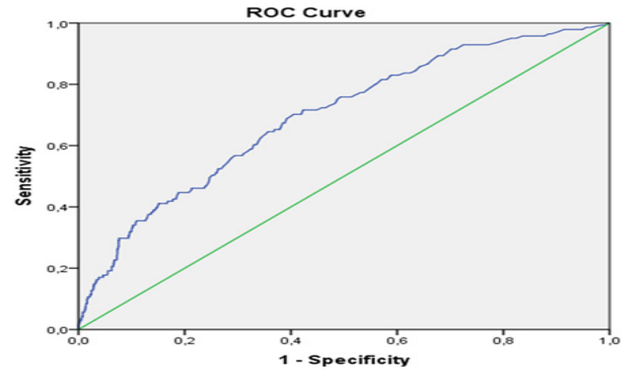

Figure 1. ROC analysis for D-dimer values between deceased and surviving patient groups

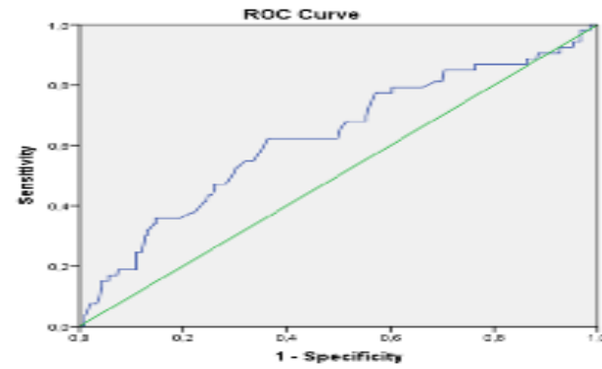

Figure 2. ROC analysis for fibrinogen values between deceased and surviving patient groups

Table 3. Comparison of the data of COVID-19 patients with and without fibrinogen elevation (n=438)

	Absence of fibrinogen elevation (n:291)	Presence of fibrinogen elevation (n:147)	P-value
Age, median (IQR 25-75)	62 (52-70)	66 (57-74)	0.22
Gender n (%)			
Female	143 (49.1%)	65 (44.2%)	0.330
Comorbidity, n (%)			
Hypertension	140(48.1%)	71 (48.3%)	0.97
Diabetes	79 (27.1%)	51 (34.7%)	0.103
Coronary heart disease	60 (20.6%)	37 (25.2%)	0.279
Chronic obstructive pulmonary disease	32 (11%)	24 (16.3%)	0.115
Chronic kidney disease	11 (3.8%)	10 (6.8%)	0.162
Vital signs, median (IQR 25-75)			
Fever	37.1 (36.3-38)	37.2 (36.3-38)	0.523
Pulse rate	78 (71-88)	78 (72-86)	0.734
Saturation	90 (88-92)	90 (89-93)	0.055
Symptom duration, median (IQR 25-75)	4 (3-6)	5 (3-6)	0.25
Pneumonic involvement more than 50%, n (%)	102 (35.1%)	41 (27.9%)	0.131
Requirement of mechanical ventilation, n (%)	38 (13.1%)	16 (10.9%)	0.513
Length of hospital stay median (IQR 25-75)	8 (6-12)	10 (6-14)	0.96
Requirement of ICU care, n (%)	45 (15.5%)	20 (13.6%)	0.605
Length of stay in ICU median (IQR 25-75)	12 (4.5-25.5)	16.5 (6-23.5)	0.464
In-hospital mortality n (%)	37 (12.7%)	16 (10.9%)	0.579

ICU: Intensive care unit

AUC value of 0.582 (95% CI 0.524-0.641) (Figure 2). A fibrinogen level of 730 that was accepted as the best cut-off value for distinguishing between deceased and surviving patients had a sensitivity of 11.7% and a specificity of 91.5%. As compared with patients without elevated fibrinogen level, those with an elevated fibrinogen level had a higher median age and a longer symptom duration ($p<0.05$ for both comparisons) (Table 3).

Discussion

In the COVID-19 pandemic, the number of patients presented to healthcare facilities or hospitals has been increasing, hospital capacities have been exceeded, and in particular, patient requirement for intensive care support has been rising. Thus, there is a growing need for developing early and effective predictors of clinical outcomes in order to risk stratify COVID-19 patients. In the present study, where we investigated how D-dimer and fibrinogen elevation would affect the mortality rate of hospitalized COVID-19 patients, we reached two basic conclusions. Firstly, we determined that deceased patients had higher admission and follow-up D-dimer levels compared with survivors. We also found that patients with D-dimer level elevation were older, had a higher rate of chronic kidney disease, higher body temperature and pulse rate, and lower oxygen saturation. We also demonstrated that these patients presented to the hospital later, had more severe pneumonia, longer hospital stay, and greater need for mechanical ventilation and intensive care. Secondly, when we analyzed our patients' fibrinogen levels, we revealed that deceased patients had an approximately 2 times higher fibrinogen level than surviving ones. However, although the results of ROC analysis that we performed to determine a cutoff value for fibrinogen that would discriminate between the deceased and surviving patients were statistically significant, it did not yield clinically meaningful results. Even though several studies in the literature have reported that elevated fibrinogen levels were associated with poor prognosis in hospitalized patients, our results were not indicative of a relationship between follow-up fibrinogen levels and mortality in spite of the fact that deceased patients had higher admission fibrinogen levels than survivors.

Data on abnormal coagulation parameters in COVID-19 have first surfaced in reports from China. In a study published in the early period of the pandemic it was reported that patients exhibited a longer bleeding time, 36% of patients had elevated D-dimer and increased inflammatory biomarkers, and 12% had thrombocytopenia [1]. In the first publications, particularly prothrombin time and D-dimer level have come into prominence as the markers of more severe disease [1]. It has been determined that thrombotic events are frequently encountered in patients with COVID-19, which has been shown as a poor prognostic sign in terms of disease severity. In a study on 560 patients from China, an elevated D-dimer level was found in 260 (46.4%) of patients; furthermore, it was shown that as disease severity increased, D-dimer level was elevated proportionally [2]. D-dimer represents the activation of coagulation and fibrinolysis systems [11]. D-dimer test is used clinically to exclude deep vein thrombosis (DVT) and pulmonary embolism (PE) and to confirm disseminated intravascular coagulation [12,13]. Elevated D-dimer levels are not only found in thromboembolic events, but also in physiological states like pregnancy and disease states such as cancer, inflammation, and surgery [14]. A review of D-dimer level in COVID-19 infection concluded that particularly diabetics and patients suffering a venous thromboembolism (VTE) have higher D-dimer level, independently of thromboembolic events [15-17]. Our findings are similar to the previous literature reports. Particularly patients with severe COVID-19 pneumonia and severe COVID-19 infection (evidenced by fever, tachycardia, hypoxia) had higher D-dimer levels. Another study on 138 patients found higher D-dimer levels in 26% of patients that required admission to the intensive care unit. That study also demonstrated that deceased patients had elevated D-dimer levels, progressive lymphopenia, and renal dysfunction. It was also observed by the same authors that D-dimer began to differentiate patients with poor prognosis 5 days after symptom onset [9]. We also found that COVID-19 patients with chronic renal failure (CRF) had higher D-dimer levels. Studies have shown a negative correlation between GFR and D-dimer levels, but no thromboembolic events during a 1-year follow-up of such patients [18,19]. Another study demonstrated that an admission D-dimer level of more than 2.0 μg/mL (four times increase) could effectively predict in-hospital mortality in COVID-19 patients, which suggested that D-dimer could be an early and effective marker for use to improve patient outcomes [10]. We similarly calculated a sensitivity of 42% and a specificity of 89% for a D-dimer cut-off value of 1475 (approximately 3 times normal) to distinguish between deceased and surviving patients. We detected elevated D-dimer levels independent of thromboembolic events in deceased patients.

Fibrinogen is the most abundant coagulation protein in the blood. It has a prominent role in the coagulation cascade and thrombosis. Its primary function is to form fibrin that causes coagulation, but it also actively participates in thrombocyte aggregation [20,21]. In a series of 43 patients by Ranucci et al. fibrinogen level was significantly higher in patients with severe COVID-19 infection [22]. In our fibrinogen level analysis, we found that deceased patients had higher fibrinogen levels at the time of admission. However, our ROC analysis to determine a cutoff value for fibrinogen level for distinguishing between deceased and surviving patients revealed no clinically meaningful result, although the result of the analysis was statistically significant. Although some studies have reported that elevated fibrinogen levels were associated with poor prognosis among hospitalized patients, we could not demonstrate any association between follow-up fibrinogen levels in deceased patients as compared with surviving ones. It was reported that fibrinogen increases in early disease and decreases in the subsequent days [23,24]. We think that this may be due to dynamic behavior of fibrinogen levels in COVID-19 patients.

Limitations

Our study has some limitations. Firstly, our results cannot be generalized to all centers due to the single-center nature of our study. Secondly, missing or erroneous data may have affected study results because of the retrospective nature of our study. Decisions regarding hospitalization, diagnostic tests, and treatment have shown some variations during the pandemic owing to continuously updated COVID-19 guidelines published

by the Ministry of Health of Turkey. Whereas even asymptomatic patients had been hospitalized in the first days after the declaration of the first cases of the disease in the country, the criteria for hospitalization had been changed in subsequent periods. This may have changed our results. Furthermore, COVID-19 patients who had no indication for hospitalization and who had been discharged from the emergency department with outpatient treatment were excluded. This may have affected our study results as well.

Conclusion

In our study, we demonstrated that D-dimer levels measured at admission and during follow-up were higher in deceased patients than surviving ones. We showed that patients with elevated D-dimer levels were older, had higher rates of chronic kidney disease, higher body temperature and pulse rates, lower oxygen saturation, more severe pneumonia, longer hospital stay, and higher requirement for mechanical ventilation and intensive care. We demonstrated that D-dimer elevation occurred independently of thromboembolic complications. Although we also demonstrated that fibrinogen levels were higher in deceased patients, we did not detect any clinical association between admission and follow-up fibrinogen levels and mortality in deceased patients as compared with surviving ones.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

References

1. Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet. 2020;395(10223):507-13.

2. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med. 2020;382(18):1708-20.

3. Wendelboe AM, Raskob GE. Global burden of thrombosis: epidemiologic aspects. Circ Res. 2016;118(9):1340–7

4. Fogarty H, Townsend L, Ni Cheallaigh C, Bergin C, Martin-Loeches I, Browne P, et al. COVID19 coagulopathy in Caucasian patients. Brit J Haematol. 2020;189(6):1044–9.

5. Chen R, Sang L, Jiang M, Yang Z, Jia N, Fu W, et al. Longitudinal hematologic and immunologic variations associated with the progression of COVID-19 patients in China. J Allergy Clin Immunol. 2020;146(1):89–100.

6. Teuwen LA, Geldhof V, Pasut A, Carmeliet P. COVID-19: the vasculature unleashed. Nat Rev Immunol. 2020; 20 (7):389-91.

7. Begbie M, Notley C, Tinlin S, Sawyer L, Lillicrap D. The Factor VIII acute phase response requires the participation of NF kappa B and C/EBP. Thromb Haemost. 2000; 84 (2):216-22.

8. Magro C, Mulvey JJ, Berlin D, Nuovo G, Salvatore S, Harp J et al. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases. Transl Res. 2020; 220:1-13.

9. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020;323(11):1061-9.

10. Zhang L, Yan X, Fan Q, Liu H, Liu X, Liu Z, et al. D-dimer levels on admission to predict in-hospital mortality in patients with Covid-19. J Thromb Haemost. 2020;18(6):1324-9.

11. Gaffney PJ. Breakdown products of fibrin and fibrinogen: molecular mechanisms and clinical implications. J Clin Pathol. 1980;14:10–7.

12. Halaby R, Popma CJ, Cohen A, Chi G, Zacarkim MR, Romero G, et al. D-Dimer elevation and adverse outcomes. J Thromb Thromboly. 2015;39(1):55–9.

13. Adam SS, Key NS, Greenberg CS. D-dimer antigen: current concepts and future prospects. Blood. 2009;113(13):2878–87.

14. De Monyé W, Sanson BJ, Mac Gillavry MR, Pattynama PM, Büller HR, van den Berg-Huysmans AA, et al. Embolus location affects the sensitivity of a rapid quantitative D-dimer assay in the diagnosis of pulmonary embolism. J Respir Crit Care Med. 2002;165(3):345–8.

15. Rostami M, Mansouritorghabeh H. D-dimer level in COVID-19 infection: a systematic review. Expert Rev Hematol. 2020;13(11):1265-75.

16. Guo W, Li M, Dong Y, Zhou H, Zhang Z, Tian C, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev. 2020; e3319.

17. Yan Y, Yang Y, Wang F, Ren H, Zhang S, Shi X, et al. Clinical characteristics and outcomes of patients with severe covid-19 with diabetes. BMJ Open Diabetes Res Care. 2020;8(1):e001343.

18. Sheikh V, Ahmadpour-Saheb N, Khazaei S. Relationship between D-dimer Levels and the Glomerular Filtration Rate in Patients with Chronic Kidney Disease. Biomedical Research and Therapy. 2021; 8(11): 4695-9.

19. Gubensek J, Lolic M, Ponikvar R, Buturovic-Ponikvar J, D-dimer levels in maintenance hemodialysis patients: high prevalence of positive values also in the group without predisposing diseases. Hemodial Int.. 2016; 20 (2):198-203.

20. Fuss C, Palmaz JC, Sprague EA. Fibrinogen: structure, function, and surface interactions. J Vasc Interv Radiol. 2001;12(6):677-82.

21. Lin SY, Hsieh TF, Wei YS. Mechanical compression affecting the thermal-induced conformational stability and denaturation temperature of human fibrinogen. Int J Biol Macromol. 2005;37(3):127-33.

22. Ranucci M, Ballotta A, Di Dedda U, Baryshnikova E, Dei Poli M, Resta M, et al. The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome. J Thromb Haemost. 2020;18(7):1747-51.

23. Tang N, Li D, Wang X. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. J Thromb Haemost. 2020;18 (4):844–7.

24. Osawa I, Okamoto K, Ikeda M, Otani A, Wakimoto Y, Yamashita M, et al. Dynamic changes in fibrinogen and D-dimer levels in COVID-19 patients on nafamostat mesylate. J Thromb Thrombolysis. 2021;51(3):649-56.

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